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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,110	07/18/2003	Uri Sagman	4451.003200/RFE	4435

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,110	SAGMAN ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt of remarks filed 9/6/06 is acknowledged.

STATUS OF CLAIMS:

- Claims 1-19 are pending in the application.
- Claims 1, and 10 are amended.

STATUS OF THE OFFICE ACTION: Final

REJECTIONS:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35

U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-3, and 7, 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlanger et al. US 6593137 "Erlanger" is maintained.

Erlanger discloses a therapeutic antibody which is specific for a fullerene or derivative thereof, wherein the fullerene is selected from the group consisting of a fullerene carbon compound having from 20 to 540 carbon atoms, (col. 2, lines 15-18). Erlanger discloses that the possibility of covalent linkage between fullerenes and a specific monoclonal antibody is raised and can be tested (col. 20, lines 4-6), and explains the way of testing the linkage in (col. 20, Lines 18+).

Erlanger's disclosure still reads on the amendments to claim 1 "wherein the antigen-binding site does not bind to the C_n". Erlanger discloses that fullerene C60 was treated

as a hapten and covalently linked to bovine serum albumin (BSA) and rabbit serum albumin (RSA) in order to induce a T-dependent immune response which can lead to high affinity antibodies. Linkage to BSA and RSA was performed via an N-hydroxysuccinimide ester derivative of C60 (col. 24, line 52-57). The disclosure is clear about using a linker between the antigen-binding site and the C_H.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erlanger et al. US 6593137 (Erlanger) in view of Williams JA et al. (Targeting and therapy of human glioma xenografts in vivo using radiolabeled antibodies.) Int J Radiat Oncol Biol Phys. 1990 Sep;19(3):633-42 (hereinafter "Williams"), further in view of

Ostensen et al. US 6375931 (Ostensen).

Erlanger has been discussed partially above.

In addition to the previous discussion, Erlanger teaches that as part of his investigation three fullerene peptide derivatives halve been prepared that are highly water soluble and can bind to C60 fullerene (col. 18, lines 4-10). The pharmaceutically acceptable carrier recited in claim 5 of the instant application is obvious to people skilled in the art since most of the compounds used in treatment of diseases need a pharmaceutically acceptable carrier. In addition Erlanger offers the formula (Ho@C.sub.82)R (where R is a group inducing water solubility and Ho is the isotope metal) (col. 27, lines 13-20).

Erlanger did not disclose the Ab comprising an antigen-binding sit selected from the group recited in claim 4.

Williams disclosed radiolabeled antibodies provide a potential basis for selective radiotherapy of human gliomas. Williams used monoclonal antibodies QCI054 and ZME018, which define a tumor-associated and a second melanoma-associated antigen, respectively, demonstrate positive immunoperoxidase staining of the tumor.

Both references did not disclose the therapeutic molecule form the group paclitaxel, doxorubicin, vincristine, or cisplatin.

Because William disclosed the effectiveness of ZME-018 in treating cancers, it would have been obvious to a man skilled in the art at the time the invention was made to use ZME-018 with fullerene to therapeutically target the cancer site. The expected result would be a composition that comprises a fullerene, an anti-body, and a radioisotope to

be used in a method of treating a cancer.

Ostensen teaches preparations that may be employed as delivery agents for bioactive moieties such as therapeutic drugs (col. 18, lines 52-63). The preparations comprise fullerene C60 (col. 28, lines 27-30 and col. 33, lines 59-60). And also comprise cancer therapy molecules like cisplatin, doxorubicin hydrochloride, vincristine, and taxol (col. 17, lines 25-30), and the combination can be comprised in treating cancers like brain cancers (col. 18, line 35-37).

Instant claim 14 recite the treatment of oxidative stress disease, since Williams include gliomas in his reference, it is recognized that glioma is an oxidative stress disease (see attached: KL Tsai et al. (Mechanism of oxidative stress-induced intracellular acidosis in rat cerebellar astrocytes and C6 glioma cells), The Journal of Physiology, Vol. 502, Issue 1 161-174, 1997.

The three references did not disclose the doses for using these compounds to treat cancers or oxidative stress syndrome. However, it is within the skills of an artisan to adjust the dose according to the severity of the condition and the needs of the patient.

3. The prior art made of record is considered pertinent to applicant's disclosure. Laura L. Dugan et al. (Carboxyfullerenes as neuroprotective agents) Proc. Natl. Acad. Sci. USA Vol. 94, pp. 9434-9439, August 1997, Neurobiology. The article discloses that Crboxylic acid C60 derivatives may have attractive therapeutic properties in several acute or chronic neurodegenerative diseases.

RESPONSE TO ARGUMENTS

Claim rejection under 35 U.S.C. § 102:

Applicant's arguments filed 10/26/2004 have been fully considered but are not persuasive. Applicant argues that:

1. Erlanger is silent concerning the antibodies specific for molecules other than a fullerene or derivative thereof.

To respond to this argument: Erlanger discloses that fullerene C60 can be linked to a antigen to which can lead to high affinity antibodies. Note that claim 1 of the instant application recites a C_n-Ab where C_n is a fullerene or nanotube.

2. Erlanger's reference to a covalent linkage between fullerenes and a specific monoclonal antibody is both speculative and directed, within the context of Erlanger, to covalent linkage between a fullerene and a monoclonal antibody specific for the fullerene.

To respond: Erlanger's disclosure of a linker between fullerene and the antigen (bovine or rabbit serum), which is similar to the instant claim 1 recitation, proves that the disclosure is not speculative.

The Examiner's statement that lanthanides are recited in claims 7 and 14 is not correct.

Examiner agrees and apologizes for the confusion between the instant claims and claims of application 10/623190 for the current applicant.

Claim rejection under 35 U.S.C. § 103:

Erlanger teaches antibodies specific for fullerenes. Williams teaches the use of radiolabeled antibodies, such as ZME018, for the treatment of cancers, but makes no mention of fullerenes or non-radioisotopic therapeutic agents. Ostensen teaches therapeutic compounds, such as anti-cancer drugs, "which may if desired be coupled to a site-specific vector having affinity for specific cells, structures or pathological sites," and also teaches the use of fullerenes to produce microbubbles. Ostensen makes no mention of antibodies or antigens.

To respond to Applicant's argument, it is noted that Erlanger teaches antigens bound covalently to fullerene. Williams disclosed radiolabeled antibodies provide a potential basis for selective radiotherapy of human gliomas. Williams used monoclonal antibodies QCI054 and ZME018. Ostensen teaches preparations that may be employed as delivery agents for bioactive moieties such as therapeutic drugs. The preparations comprise fullerene C60 and cancer therapy molecules like cisplatin, doxorubicin hydrochloride, vincristine, and taxol. The three references teach every limitation of the instant application.

Applicant finally argues that no combination or modification of Erlanger, Williams, and Ostensen can render the present claims obvious. Williams teaches the use of radiolabeled antibodies to treat cancer, but provides neither motivation nor any expectation of success for the skilled artisan to use non- radioisotopic therapeutic agents, alone or in conjunction with fullerenes, to treat cancer.

Accordingly, it would have been obvious to one of ordinary skills in art at the time the invention was made to combine Erlanger to William because William disclosed the

effectiveness of ZME-018 in treating cancers, and to use ZME-018 with fullerene to therapeutically target the cancer site. The skilled artisan would be motivated also to add an antitumor drug because it results into better potentially treatment for a cancer. The expected result would be a composition that comprises a fullerene, an anti-body, and a radioisotope to be used in a method of treating a cancer.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim 10/25/06

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER